

CLAIMS

1. Use of a substance for the manufacture of a medicament for the treatment and/or prevention of a fibrotic disease, wherein the substance is selected from the group consisting of:
 - a) A polypeptide comprising SEQ ID NO: 2 or SEQ ID NO: 4;
 - b) A polypeptide comprising amino acids 22 to 401 of SEQ ID NO: 2 or SEQ ID NO: 4;
 - c) A polypeptide comprising one, two, three or four cysteine-rich domains of osteoprotegerin;
 - d) A polypeptide comprising amino acids 22 to 194 of SEQ ID NO: 2 or SEQ ID NO: 4;
 - e) A mutein of any of (a) to (d), wherein the amino acid sequence has at least 40 % or 50 % or 60 % or 70 % or 80 % or 90 % identity to at least one of the sequences in (a) to (d);
 - f) A mutein of any of (a) to (d) which is encoded by a DNA sequence which hybridizes to the complement of the DNA sequence encoding any of (a) to (d) under moderately stringent conditions or under highly stringent conditions;
 - g) A mutein of any of (a) to (d) wherein any changes in the amino acid sequence are conservative amino acid substitutions to the amino acid sequences in (a) to (d);
 - h) a salt or an isoform, fused protein, functional derivative, active fraction or circularly permuted derivative of any of (a) to (g).
2. Use according to claim 1, wherein the fibrotic disease is a connective tissue disease.
3. Use according to claim 1 or 2, wherein the fibrotic disease is scleroderma.
4. Use according to any preceding claims, wherein the substance is a monomer or dimer.
5. Use according to any preceding claims, wherein the substance is glycosylated at one or more sites.
6. Use according to any of the preceding claims, wherein the fused protein comprises an immunoglobulin (Ig) fusion.

7. Use according to claim 6, wherein the Ig fusion is an Fc fusion.
8. Use according to any of the preceding claims, wherein the functional derivative comprises at least one moiety attached to one or more functional groups, which occur as one or more side chains on the amino acid residues.
9. Use according to claim 8, wherein the moiety is a polyethylene moiety.
10. Use of a nucleic acid molecule for manufacture of a medicament for the treatment and/or prevention of a fibrotic disease, wherein the nucleic acid molecule comprises a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the group consisting of:
 - a) A polypeptide comprising SEQ ID NO: 2 or SEQ ID NO: 4;
 - b) A polypeptide comprising amino acids 22 to 401 of SEQ ID NO: 2 or SEQ ID NO: 4;
 - c) A polypeptide comprising one, two, three or four cytein-rich domains of osteoprotegerin;
 - d) A polypeptide comprising amino acids 22 to 194 of SEQ ID NO: 2 SEQ ID NO: 4;
 - e) A mutein of any of (a) to (d), wherein the amino acid sequence has at least 40 % or 50 % or 60 % or 70 % or 80 % or 90 % identity to at least one of the sequences in (a) to (d);
 - f) A mutein of any of (a) to (d) which is encoded by a DNA sequence which hybridizes to the complement of the native DNA sequence encoding any of (a) to (d) under moderately stringent conditions or under highly stringent conditions;
 - g) A mutein of any of (a) to (d) wherein any changes in the amino acid sequence are conservative amino acid substitutions to the amino acid sequences in (a) to (d);
 - h) An isoform, fused protein or active fraction of any of (a) to (g).
11. Use according to claim 10, wherein the fibrotic disease is a connective tissue disease.
12. Use according to claim 10 or 11, wherein the fibrotic disease is scleroderma.

13. Use according to any of claims 10 to 12, wherein the nucleic acid molecule comprises an expression vector sequence.
14. Use according to claim 13, wherein the vector sequence is a gene therapy vector sequence.
15. Use of a vector for inducing and/or enhancing the endogenous production of a polypeptide according to claim 1 in a cell for the preparation of a medicament for the treatment and/or prevention of a fibrotic disease, in particular scleroderma.
16. Use of a cell comprising a nucleic acid molecule according to any of claims 10 to 15 for the preparation of a medicament for the treatment and/or prevention of fibrotic disease, in particular scleroderma.
17. Use of a cell expressing a substance according to claim 1 to 9 for the manufacture of a medicament for the treatment and/or prevention of a fibrotic disease, in particular scleroderma.
18. Use of a cell that has been genetically modified to produce a polypeptide according claim 1 to 9 for the manufacture of a medicament for the treatment and/or prevention of a fibrotic disease, in particular scleroderma.
19. The use according to any of the preceding claims, wherein the medicament further comprises an interferon, for simultaneous, sequential, or separate use.
20. The use according to claim 19, wherein the interferon is interferon- β .
21. The use according to any of the preceding claims, wherein the medicament further comprises a Tumor Necrosis Factor (TNF) antagonist for simultaneous, sequential, or separate use.
22. The use according to claim 21, wherein the TNF antagonist is TBPI and/or TBPII.
23. The use according to any of the preceding claims, wherein the medicament further comprises an anti-scleroderma agent for simultaneous, sequential, or separate use.

24. The use according to claim 25, wherein the anti-scleroderma agent is selected from the group consisting of halofuginone, ACE inhibitors, calcium channel blockers, proton pump inhibitors, NSAIDs, COX-inhibitors, corticosteroids, tetracycline, pentoxifylline, bucillamine, geranylgeranyl transferase inhibitors, rotterlin, prolyl-4-hydroxylase inhibitors, c-proteinase inhibitors, lysyl-oxidase inhibitors, relaxin, halofuginone, prostaglandins, prostacyclins, endothelin-1, nitric oxide, angiotensin II inhibitors, anti-oxidants or SARP-1.
25. Method for treating and/or preventing a fibrotic disease, in particular scleroderma, comprising administering to a patient in need thereof an effective amount of a substance according to any of claims 1 to 24, optionally together with a pharmaceutically acceptable carrier.